Remarks

The invention encompasses an expression cassette having a fiber-specific promoter, such as the E6 promoter, driving expression of a gene encoding an elastic and plastic protein based polymer, preferably having the repetitive amino acid sequence Gly-Val-Gly-Val-Pro (SEQ. ID. NO. 2), a terminator, selectable marker genes, and regulatory elements for transforming plant cells and a transgenic cotton plant having fiber cells stably transformed therewith which cells exhibit improved physical and chemical properties.

We note with appreciation the cancellation of Claims 1-2 from the first of two sets of claims as requested. Claims 1-7 are present in the case, Claim 7 being added herewith, as supported by paragraph [0010] of the Substitute Specification.

A Substitute Specification conforming to the formatting requirements and including a brief description of drawings, an abstract, sequence identification numbers and paragraph numbering is submitted herewith. Former paragraph numbers [0015], [0011] and [0012] have been relocated to paragraph positions [0008.1], [0008.6], and [0009.1], respectively, to improve readability. The drawings have been omitted from the text of the Specification. Copies of the drawings are submitted herewith on separate sheets of paper. Formal drawings will be submitted upon an indication of allowability of the claims. No new matter has been added.

35 U.S.C. §112

Claims 1 and 2 have been amended to clarify that the fiber cells are stably transformed with an expression cassette having a gene encoding an elastic and plastic protein based polymer. Zhang, et al. (1995, Biotechnology Lett. 17:1279-1284) (hereinafter "Zhang 1995") is directed to the expression of a protein based polymer gene in *tobacco* cells which were transformed by particle bombardment. Zhang 1995 notes that the amount of the polymer protein detected by Western blot analysis and ELISA is much less than expected

from the level of mRNA detected by Northern blot. Zhang 1995 hypothesizes that this may be a result of using a prokaryote preferred codon composition. Therefore, this invention proposes enhancing the level of polymer production by modifying the codon composition to a plant nuclear preferred codon composition. Zhang 1995 also postulates that limited availability of amino acids may be a factor contributing to low level expression of the polymer. That reference suggests that this may be overcome by culturing cells in media supplemented with amino acids. Additionally, experiments conducted subsequent to the Zhang 1995 study revealed that, while lower levels of expression were observed in cultured tobacco cells and some transgenic plants in the F_0 generation, higher levels of protein expression were observed in transgenic plants after self-crossing, as explained in paragraph [0010] of the Specification. Furthermore, inclusion bodies were observed in tobacco cells, as shown in Figure 2 of the Specification, thus indicating high levels of protein expression. These results support the conclusion that protein expression in plants is successful, as demonstrated by Western blot and ELISA analyses. Analysis of the chemical and physical properties of the plants, including water absorption, thermal characteristics, fiber strength, and dye binding capacity is not necessary to show expression of the protein. Furthermore, methods of evaluation of these properties are well-known in the art and thus do not require undue experimentation. In light of this evidence, we respectfully submit that one skilled in the art would readily anticipate expression of the protein-based polymer in plants. Therefore, we request that the unpredictability-based objection to Claims 1 and 2 be withdrawn.

Claim 6 has been amended to depend from Claim 3. Accordingly, the polymer is characterized as an *elastic and plastic* protein based polymer, as supported by paragraph [0009] of the Specification. Likewise, Claims 1-4 have been amended to characterize the gene as that encoding an *elastic and plastic* protein based polymer.

As stated in *University of California v. Eli Lilly*, 43 U.S.P.Q. 2d 1398 (Fed. Cir. 1997), an adequate written description of the genus defines "structural features commonly possessed by members of the genus that distinguish them from others". The characterization of the gene of the amended claims does just that. In other words, an elastic and plastic protein polymer is characterized as having a repeating peptide sequence and as exhibiting both elastic and plastic qualities at differing temperatures. Such a peptide sequence is a series of amino acid repeats, which thus defines the structure of the nucleic acid encoding therefor. Thus, one skilled in the art can recognize the identity of the members of the genus of genes so as to distinguish them from other genes. Additionally, the Specification provides two examples of the genus: VPGVG and GVGVP. Furthermore, unlike the cases of *Eli Lilly* and *Amgen Inc. v. Chugai Pharmaceutical*, 18 U.S.P.Q. 2d 1016 (Fed. Cir. 1991), the claims at issue are not directed to a gene *per se*. Instead, the claims encompass *an expression cassette* having the described gene as one of its components, and to a transgenic cotton plant having fiber cells transformed therewith. Thus, we respectfully submit that amendments to Claims 1-4 and 6 describing the gene component of the expression cassette provide sufficient characterization of the invention to overcome the rejection based on lack of written description.

Claim 1 has been amended to clarify that it is the fiber cells that exhibit the claimed properties, as supported in the Specification by paragraph [0006]. The phrase "chemical reactivity" has been omitted in favor of "elasticity and dye binding capacity", as supported by paragraph [0008.1] (formerly paragraph [0011]) of the Specification. Furthermore, the phrase "thermal characteristics" has been omitted from Claim 1. Claim 7 has been added to clarify that the protein based polymer exhibits temperature transition at a temperature lower than body temperature as supported by paragraph [0009.1] of the Specification. The term "improved" has been amended to "increased" to clarify that water absorption, elasticity,

dye binding capacity, and fiber strength of the transformed fiber cells is greater than that of untransformed cells. Additionally, the term "including" has been deleted from and the term "and" has been inserted into Claim 1. Thus, we respectfully submit that Claims 1 and 7 as amended satisfy 35 U.S.C. §112, first paragraph.

Claim 6 has been amended to provide clear antecedent basis for each of the claim elements. Claim 6 has further been amended to clarify that it is drawn to the expression cassette of Claim 3 having a synthetic gene that is not found in nature wherein manipulation of the gene sequence allows control of the physical and/or chemical properties of the protein based polymer, as supported by paragraph [0014] of the Specification.

Claims 5 and 6 have been amended to replace "As" with "The". The phrase "balanced by" has been deleted from Claim 3. Additionally, regulatory elements are simply specified as additional components of the claimed expression cassette. As such, we respectfully submit that inserting "and" after "terminator" is unnecessary. Claim 3 has been further amended to clarify that the promoter drives the expression of the gene encoding the polymer and to provide clear antecedent basis for each element.

In Claims 2 and 4, the term "contains" has been replaced with "comprises". Additionally, those claims as amended recite the SEQ. ID. NO. corresponding to the amino acid pentamer.

Claim 4 has been further amended to clarify that the elastic and plastic protein based polymer comprises the recited repetitive amino acid sequence. The phrase "the gene" has thus been omitted from the claim.

Art-based Rejections

The Examiner first relies upon Zhang, et al. (1996, Plant Cell Rep. 16: 174-179) (hereinafter "Zhang 1996") and Daniell, et al. (U.S. Patent No. 6,004,782) (hereinafter "Daniell '782") in making rejections to Claim 6 under 35 U.S.C. §102. Claim 6 as amended

is directed to an expression cassette having a fiber specific promoter driving expression of a synthetic gene encoding an elastic and plastic protein based polymer, a terminator, one or more selectable marker genes, and one or more regulatory elements wherein manipulation of the gene sequence provides control of the physical and/or chemical properties of the protein based polymer. Both Zhang 1996 and Daniell '782 fail to mention a fiber specific promoter. Thus, Claim 6 as amended is patentably distinct over those references.

Claims 1, 3 and 5-6 are rejected under §102(b) over U.S. Patent No. 5,602,321 to John et al. (hereinafter "John '321") and over John, et al. (1996, Proc. Natl. Acad. Sci. USA 93: 12768-12773) (hereinafter "John 1996"). Amended Claims 1, 3 and 5-6 encompass an expression cassette having a gene encoding an elastic and plastic protein based polymer and transgenic cotton plants having fiber cells stably transformed therewith. John '321 does not require that the encoded protein be an elastic and plastic protein based polymer. Additionally, John 1996 fails to mention a gene encoding an elastic and plastic protein based polymer. Rather, John '321 and John 1996 teach a multigene construct encoding *bioplastic-producing enzymes* which *process* a polyester, specifically polyhydroxybutyrate. In other words, the plastic is biosynthesized by the encoded enzymes; the construct itself does not encode the protein-based polymer. As such, amended Claims 1, 3 and 5-6 are patentably distinct over both John '321 and John 1996.

We further respectfully submit that Claims 1-3 and 5-6 as amended are patentably distinguishable over U.S. Patent No. 5,597,718 to John, et al. (hereinafter "John '718") in light of John et al. (1995, Plant Physiology 108: 669-676) (hereinafter "John 1995"). As stated above, Claims 1-3 and 5-6 as amended are drawn to an expression cassette containing, among other things, a fiber specific promoter driving expression of a synthetic gene encoding an elastic and plastic protein based polymer. Neither John '718 nor John 1995 provides any evidence that the naturally occurring H6 protein is an elastic and plastic protein based

polymer, regardless of the fact that the H6 protein contains a pentameric repeat. Furthermore, the record is utterly devoid of any evidence to support the conclusion that the protein would confer improved water absorption, thermal characteristics and chemical reactivity to the transformed fiber cells or that the transgenic plants would contain a protein having a GVGVP repeat. Thus, we respectfully submit that the invention as defined by Claims 1-3 and 5-6 is patentably distinct over John '718 and John 1995.

We further respectfully submit that Claims 1-6 are patentable over John '718 and Zhang 1996. Claims 1 and 2 encompass a transgenic cotton plant comprising fiber cells stably transformed with an expression cassette having a gene encoding an elastic and plastic protein based polymer wherein said fiber cells exhibit increased water absorption, fiber strength, elasticity, and dye binding capacity. Claims 3-6 are directed to an expression cassette having a fiber-specific promoter, a gene encoding an elastic and plastic protein based polymer, a terminator, one or more selectable marker genes, and regulatory elements.

John '718 discloses a construct having an E6 promoter, H6 gene, and selection markers and cotton plants transformed therewith to genetically engineer cotton fiber. John '718, however, does not teach or suggest a gene encoding $(GVGVP)_n$. Zhang 1996 reports the expression of a gene encoding a protein based polymer $(GVGVP)_{121}$ in transgenic tobacco plants. The objective of Zhang 1996 is to provide a commercially viable production method for protein based polymers which are useful, biodegradable materials. In sharp contrast to this invention, neither reference teaches or suggests that the presence of a plastic and elastic protein based polymer in the plant improves the properties of the transgenic plant itself, such as dye binding capacity, elasticity, strength, and water absorption. Therefore, we respectfully submit that, absent the Applicants' disclosure, no motivation to combine John '718 and Zhang 1996 existed at the time of the invention. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior

art also suggests the desirability of the combination. *See* In re Mills, 16 U.S.P.Q. 2d 1430 (Fed. Cir. 1990). Impermissible hindsight analysis must be avoided. In view of the lack of motivation to combine the references, no prima facie case of obviousness has been established.

Furthermore, we respectfully submit that any hypothetical combination of John '718 and Zhang 1996 does not amount to the invention. Any hypothetical combination of Zhang 1996 and John '718 when those references are considered as a whole as required by 35 U.S.C. §103, results in a transgenic plant having cells transformed with a construct having an E6 promoter, an H6 gene, a gene encoding $(GVGVP)_{121}$, and selectable markers. In sharp contrast, the expression cassette of this invention improves the properties of the transgenic plant using a single gene encoding that elastic and plastic protein based polymer, a factor weighing in favor of nonobviousness.

Additionally, neither reference teaches or suggests that expression of a gene encoding a plastic and elastic protein based polymer in a cotton plant would enhance the qualities of the cotton fiber cell, including fiber strength, elasticity, dye binding capacity, and water absorption, as recited in Claim 1. One having skill in the art would not have expected these results in view of the teachings of the prior art, thus lending further support to the non-obviousness of the invention. *See* MPEP §716.02(a).

Further, obviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established. *See* In re Rickjaert, 28 U.S.P.Q. 2d 1955 (Fed. Cir. 1993). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, *and that it would be so recognized by persons of ordinary skill.* Inherency, however, may not be established by probabilities of possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" *In*

re Robertson, 49 U.S.P.Q. 2d 1949, 1950-51 (Fed. Cir. 1999) (emphasis added). There is simply no evidence on this record that one of skill in the art would have recognized the claimed cotton properties at the time of the invention absent Applicants' disclosure.

In view of the differences between the claimed invention and any hypothetical combination of John '718 and Zhang 1996, we respectfully submit that the invention is patentably distinct over the cited prior art.

Similarly, we respectfully submit that any hypothetical combination of John 1996 and Zhang 1996 cannot preclude patentability of the solicited claims. John 1996 discloses a construct having an E6 promoter, *pha B* and *phaC* genes, and selectable markers but makes no mention of a gene encoding an elastic and plastic protein based polymer. Zhang 1996 reports the expression of a gene encoding a protein based polymer $(GVGVP)_{121}$ in transgenic tobacco plants. Again, however, neither John 1996 nor Zhang 1996 teaches or suggests that the presence of a plastic and elastic protein based polymer in the plant improves the properties of the transgenic plant itself. Thus, no motivation to combine the references existed at the time of the invention, and, hence, no *prima facie* case of obviousness has been established on this record.

We further respectfully submit that any hypothetical combination of John 1996 and Zhang 1996 when those references are considered as a whole as required by 35 U.S.C. §103, results in a transgenic plant having cells transformed with a construct having an E6 promoter, *phaB* and *phaC* genes, a gene encoding $(GVGVP)_{121}$, and selectable markers. The expression cassette of the invention achieves the improved properties using just a single gene encoding $(GVGVP)_n$, thus weighing in favor of nonobviousness.

Additionally, neither John 1996 nor Zhang 1996 teaches or suggests that expression of a gene encoding an elastic and plastic protein based polymer in a cotton plant would enhance the qualities of the cotton fiber cell, including fiber strength, elasticity, dye binding

capacity, and water absorption, as recited in Claim 1. One having skill in the art would not have expected these results in view of the teachings of the prior art, thus lending further support to the nonobviousness of the invention.

Further, as previously stated, obviousness cannot be predicated on what is not known at the time the invention is made, even if the inherency of a certain feature is later established. *See* In re Rickjaert, *supra*.

In light of these differences, we respectfully submit that the claims are patentably distinct over the cited hypothetical combination of prior art references.

In view of the foregoing, we respectfully submit that the application is in condition for allowance, which early action is requested.

Respectfully submitted,

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